

REMARKS

Applicants enclose herewith the Sequence Listing for the above-captioned application and a 3.5" floppy disk containing the Sequence Listing.

The specification has been amended to provide SEQ ID NO for the sequence disclosed therein. This submission contains no new matter.

I hereby state that the content of the paper and computer readable copies of the Sequence Listing, submitted in accordance with 37 CFR § 1.821(c) and (e), respectively, are the same.

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: 19 June 2001

Valeta A. Gregg
Valeta A. Gregg, Reg. No. 35,12707
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, NY 10174-6401
(212) 867-0123



23650

PATENT TRADEMARK OFFICE



Marked Up Version Showing Changes Made

Glucagon-like peptide-1, also referred to as GLP-1, is a peptide sequence found in the C-terminal portion of mammalian proglucagon. Prior to 1985, no definite biological activity of GLP-1 had been reported. However, in 1985 it was demonstrated that the amide of a fragment of GLP-1, namely GLP-1(1-36)amide, stimulates insulin release from isolated precultured rat pancreatic islets in the presence of glucose in a dose-dependent manner (Schmidt, W.E. et al. *Diabetologia* 28 (1985) 704-7). This finding suggests that GLP-1(1-36)amide and related peptides might be useful in the treatment of type 2 diabetes. Due to its substantially closer sequence homology to glucagon and glucosedeprived insulinotropic peptide, also referred to as GIP, Schmidt et al. suggested that an even stronger glucagon- and/or GIP-like biological activity could be expected with GLP-1(7-36) than with the intact peptide. In recent years, particular interest has focused on the GLP-1 fragments GLP-1(7-37) and GLP-1(7-36)amide and analogues and functional derivatives thereof. The designation GLP-1(1-36) indicates that the peptide fragment in question comprises the amino acid residues from (and including) number 1 to (and including) number 36 when counted from the N-terminal end of the parent peptide, GLP-1. Similarly, the designation GLP-1(7-37) designates that the fragment in question comprises the amino acid residues from (and including) number 7 to (and including) number 37 when counted from the N-terminal end of the parent peptide, GLP-1. The amino acid sequence of GLP-1(7-36)amide and of GLP-1(7-37) is given in formula I (SEQ ID NO:1):

His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-
Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-
Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-X
(I)

which shows GLP-1(7-36)amide when X is NH₂ and GLP-1(7-37) when X is Gly-OH.